# Avian influenza - fact sheet

**15 January 2004**

Further to the previous report on avian influenza, WHO has issued a fact sheet about the significance for human health of avian influenza.

## Avian influenza ("bird flu") and the significance of its transmission to humans

### The disease in birds: impact and control measures

Avian influenza is an infectious disease of birds caused by type A strains of the influenza virus. The disease, which was first identified in Italy more than 100 years ago, occurs worldwide.

All birds are thought to be susceptible to infection with avian influenza, though some species are more resistant to infection than others. Infection causes a wide spectrum of symptoms in birds, ranging from mild illness to a highly contagious and rapidly fatal disease resulting in severe epidemics. The latter is known as "highly pathogenic avian influenza". This form is characterized by sudden onset, severe illness, and rapid death, with a mortality that can approach 100%.

Fifteen subtypes of influenza virus are known to infect birds, thus providing an extensive reservoir of influenza viruses potentially circulating in bird populations. To date, all outbreaks of the highly pathogenic form have been caused by influenza A viruses of subtypes H5 and H7.

Migratory waterfowl – most notably wild ducks – are the natural reservoir of avian influenza viruses, and these birds are also the most resistant to infection. Domestic poultry, including chickens and turkeys, are particularly susceptible to epidemics of rapidly fatal influenza.

Direct or indirect contact of domestic flocks with wild migratory waterfowl has been implicated as a frequent cause of epidemics. Live bird markets have also played an important role in the spread of epidemics.

Recent research has shown that viruses of low pathogenicity can, after circulation for sometimes short periods in a poultry population, mutate into highly pathogenic viruses. During a 1983–1984 epidemic in the United States of America, the H5N2 virus initially caused low mortality, but within six months became highly pathogenic, with a mortality approaching 90%. Control of the outbreak required destruction of more than 17 million birds at a cost of nearly US$ 65 million. During a 1999–2001 epidemic in Italy, the H7N1 virus, initially of low pathogenicity, mutated within 9 months to a highly pathogenic form. More than 13 million birds died or were destroyed.

The quarantining of infected farms and destruction of infected or potentially exposed flocks are standard control measures aimed at preventing spread to other farms and eventual establishment of the virus in a country's poultry population. Apart from being highly contagious, avian influenza viruses are readily transmitted from farm to farm by mechanical means, such as by contaminated equipment, vehicles, feed, cages, or clothing. Highly pathogenic viruses can survive for long periods in the environment, especially when temperatures are low. Stringent sanitary measures on farms can, however, confer some degree of protection.

In the absence of prompt control measures backed by good surveillance, epidemics can last for years. For example, an epidemic of H5N2 avian influenza, which began in Mexico in 1992, started with low pathogenicity, evolved to the highly fatal form, and was not controlled until 1995.

**A constantly mutating virus: two consequences**

All type A influenza viruses, including those that regularly cause seasonal epidemics of influenza in humans, are genetically labile and well adapted to elude host defenses. Influenza viruses lack mechanisms for the “proofreading” and repair of errors that occur during replication. As a result of these uncorrected errors, the genetic composition of the viruses changes as they replicate in humans and animals, and the existing strain is replaced with a new antigenic variant. These constant, permanent and usually small changes in the antigenic composition of influenza A viruses are known as antigenic “drift”.

The tendency of influenza viruses to undergo frequent and permanent antigenic changes necessitates constant monitoring of the global influenza situation and annual adjustments in the composition of influenza vaccines. Both activities have been a cornerstone of the WHO Global Influenza Programme since its inception in 1947.

Influenza viruses have a second characteristic of great public health concern: influenza A viruses, including subtypes from different species, can swap or “reassort” genetic materials and merge. This reassortment process, known as antigenic “shift”, results in a novel subtype different from both parent viruses. As populations will have no immunity to the new subtype, and as no existing vaccines can confer protection, antigenic shift has historically resulted in highly lethal pandemics. For this to happen, the novel subtype needs to have genes from human influenza viruses that make it readily transmissible from person to person for a sustainable period.

Conditions favourable for the emergence of antigenic shift have long been thought to involve humans living in close proximity to domestic poultry and pigs. Because pigs are susceptible to infection with both avian and mammalian viruses, including human strains, they can serve as a “mixing vessel” for the scrambling of genetic material from human and avian viruses, resulting in the emergence of a novel subtype. Recent events, however, have identified a second possible mechanism. Evidence is mounting that, for at least some of the 15 avian influenza virus subtypes circulating in bird populations, humans themselves can serve as the “mixing vessel”.

**Human infection with avian influenza viruses: a timeline**

Avian influenza viruses do not normally infect species other than birds and pigs. The first documented infection of humans with an avian influenza virus occurred in Hong Kong in 1997, when the H5N1 strain caused severe respiratory disease in 18 humans, of whom 6 died. The infection of humans coincided with an epidemic of highly pathogenic avian influenza, caused by the same strain, in Hong Kong’s poultry population.

Extensive investigation of that outbreak determined that close contact with live infected poultry was the source of human infection. Studies at the genetic level further determined that the virus had jumped directly from birds to humans. Limited transmission to health care workers occurred, but did not cause severe disease.

Rapid destruction – within three days – of Hong Kong’s entire poultry population, estimated at around 1.5 million birds, reduced opportunities for further direct transmission to humans, and may have averted a pandemic.

That event alarmed public health authorities, as it marked the first time that an avian influenza virus was transmitted directly to humans and caused severe illness with high mortality. Alarm mounted again in February 2003, when an outbreak of H5N1 avian influenza in Hong Kong caused 2 cases and 1 death in members of a family who had recently travelled to southern China. Another child in the family died during that visit, but the cause of death is not known.

Two other avian influenza viruses have recently caused illness in humans. An outbreak of highly pathogenic H7N7 avian influenza, which began in the Netherlands in February 2003, caused the death of one veterinarian two months later, and mild illness in 83 other humans. Mild cases of avian influenza H9N2 in children occurred in Hong Kong in 1999 (two cases) and in mid-December 2003 (one case). H9N2 is not highly pathogenic in birds.

The most recent cause for alarm occurred in January 2004, when laboratory tests confirmed the presence of H5N1 avian influenza virus in human cases of severe respiratory disease in the northern part of Viet Nam.

**Why H5N1 is of particular concern**

Of the 15 avian influenza virus subtypes, H5N1 is of particular concern for several reasons. H5N1 mutates rapidly and has a documented propensity to acquire genes from viruses infecting other animal species. Its ability to cause severe disease in humans has now been documented on two occasions. In addition, laboratory studies have demonstrated that isolates from this virus have a high pathogenicity and can cause severe disease in humans. Birds that survive infection excrete virus for at least 10 days, orally and in faeces, thus facilitating further spread at live poultry markets and by migratory birds.

The epidemic of highly pathogenic avian influenza caused by H5N1, which began in mid-December 2003 in the Republic of Korea and is now being seen in other Asian countries, is therefore of particular public health concern. H5N1 variants demonstrated a capacity to directly infect humans in 1997, and have done so again in Viet Nam in January 2004. The spread of infection in birds increases the opportunities for direct infection of humans. If more humans become infected over time, the likelihood also increases that humans, if concurrently infected with human and avian influenza strains, could serve as the “mixing vessel” for the emergence of a novel subtype with sufficient human genes to be easily transmitted from person to person. Such an event would mark the start of an influenza pandemic.

**Influenza pandemics: can they be averted?**

Based on historical patterns, influenza pandemics can be expected to occur, on average, three to four times each century when new virus subtypes emerge and are readily transmitted from person to person. However, the occurrence of influenza pandemics is unpredictable. In the 20th century, the great influenza pandemic of 1918–1919, which caused an estimated 40 to 50 million deaths worldwide, was followed by pandemics in 1957–1958 and 1968–1969.

Experts agree that another influenza pandemic is inevitable and possibly imminent.

Most influenza experts also agree that the prompt culling of Hong Kong’s entire poultry population in 1997 probably averted a pandemic.

Several measures can help minimize the global public health risks that could arise from large outbreaks of highly pathogenic H5N1 avian influenza in birds. An immediate priority is to halt further spread of epidemics in poultry populations. This strategy works to reduce opportunities for human exposure to the virus. Vaccination of persons at high risk of exposure to infected poultry, using existing vaccines effective against currently circulating human influenza strains, can reduce the likelihood of co-infection of humans with avian and influenza strains, and thus reduce the risk that genes will be exchanged. Workers involved in the culling of poultry flocks must be protected, by proper clothing and equipment, against infection. These workers should also receive antiviral drugs as a prophylactic measure.

When cases of avian influenza in humans occur, information on the extent of influenza infection in animals as well as humans and on circulating influenza viruses is urgently needed to aid the assessment of risks to public health and to guide the best protective measures. Thorough investigation of each case is also essential. While WHO and the members of its global influenza network, together with other international agencies, can assist with many of these activities, the successful containment of public health risks also depends on the epidemiological and laboratory capacity of affected countries and the adequacy of surveillance systems already in place.

While all these activities can reduce the likelihood that a pandemic strain will emerge, the question of whether another influenza pandemic can be averted cannot be answered with certainty.

**Clinical course and treatment of human cases of H5N1 avian influenza**

Published information about the clinical course of human infection with H5N1 avian influenza is limited to studies of cases in the 1997 Hong Kong outbreak. In that outbreak, patients developed symptoms of fever, sore throat, cough and, in several of the fatal cases, severe respiratory distress secondary to viral pneumonia. Previously healthy adults and children, and some with chronic medical conditions, were affected.

Tests for diagnosing all influenza strains of animals and humans are rapid and reliable. Many laboratories in the WHO global influenza network have the necessary high-security facilities and reagents for performing these tests as well as considerable experience. Rapid bedside tests for the diagnosis of human influenza are also available, but do not have the precision of the more extensive laboratory testing that is currently needed to fully understand the most recent cases and determine whether human infection is spreading, either directly from birds or from person to person.

Antiviral drugs, some of which can be used for both treatment and prevention, are clinically effective against influenza A virus strains in otherwise healthy adults and children, but have some limitations. Some of these drugs are also expensive and supplies are limited.

Experience in the production of influenza vaccines is also considerable, particularly as vaccine composition changes each year to match changes in circulating virus due to antigenic drift. However, at least four months would be needed to produce a new vaccine, in significant quantities, capable of conferring protection against a new virus subtype.